

# B Cell Acute Lymphocytic Leukemia Presenting as a Bile Duct Stricture Diagnosed With Cholangioscopy

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## ABSTRACT

Indeterminate biliary strictures represent a diagnostic challenge requiring further work-up, which encompasses a variety of diagnostic modalities. We report a very rare case of B-cell acute lymphocytic leukemia presenting as a biliary stricture following remission of acute myeloid leukemia, which was initially treated with allogenic stem cell transplant. After multiple diagnostic modalities were implemented with no success, the use of cholangioscopy-guided biopsies was the key for the final diagnosis.

## INTRODUCTION

Symptomatic bile duct strictures can result in cholestasis, which presents with jaundice, icterus, pruritus, right upper quadrant pain, and steatorrhea. Generally, biliary strictures are classified into benign, indeterminate, and malignant strictures. The majority of biliary strictures are benign, and their most common etiology include iatrogenic injuries mostly from surgical procedures, autoimmune diseases, including primary sclerosing cholangitis, and liver transplantation.<sup>1</sup> Malignant strictures derive most commonly from desmoplastic reaction in the setting of a hepatopancreaticobiliary malignancy. The most challenging biliary strictures are the indeterminate strictures, which are defined as biliary strictures with unknown etiology following cross-sectional imaging and tissue sampling. In these circumstances, significant attention needs to be drawn to the patient's history, as the nature of an obstruction is often immediately clear at the time of investigation.<sup>2</sup>

The repertoire of noninvasive and invasive studies to diagnose indeterminate strictures is broad, with varying sensitivity and specificity. Magnetic resonance imaging and magnetic resonance cholangiopancreatography are safe to diagnose whether the stricture has benign or malignant features but are hampered by the fact that tissue sampling cannot be performed. On the other hand, endoscopic retrograde cholangiopancreatography (ERCP) is an invasive procedure that allows tissue sampling to which many authors refer as the gold standard test for biliary strictures.<sup>3,4</sup> Diagnostic modalities include biliary brushing (sensitivity 57%, specificity 90%–100%), fluoroscopic-guided biopsies (sensitivity 74%, specificity 70%), fluorescence in situ hybridization (sensitivity 34%, specificity 91%), cholangioscopy with directed biopsies (sensitivity 43%–81%, specificity 90%–100%), endoscopic ultrasound with fine-needle aspiration (sensitivity 43%–89%, specificity 100%), intraductal ultrasound (sensitivity 83%–91%, specificity 50%–92%), and confocal laser endomicroscopy (sensitivity 98%, specificity 67%).<sup>4,5</sup> Combination of modalities may increase the diagnostic yield.

## CASE REPORT

A 65-year-old man presented with 1 week of fever, right upper quadrant pain, jaundice, pruritus, and subjective steatorrhea. He had a medical history of acute myeloid leukemia arising from myelodysplastic syndrome that was

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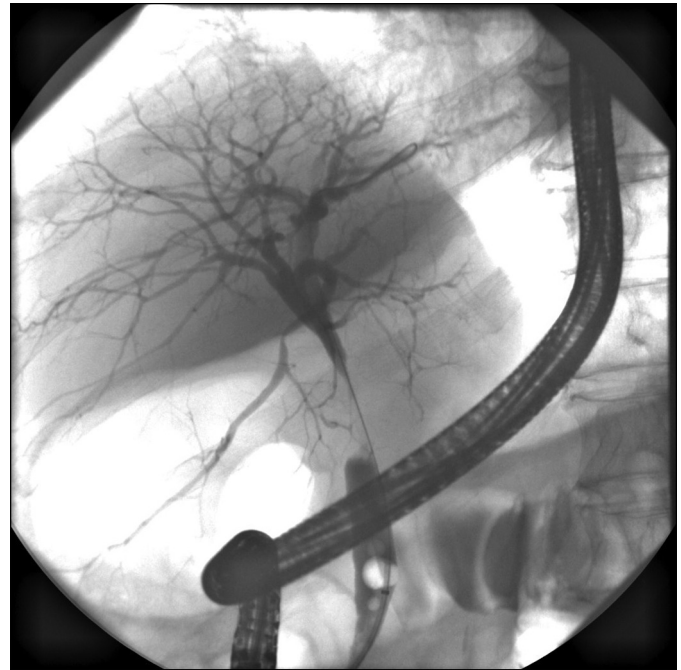


**Figure 1.** Magnetic resonance cholangiopancreatography showing narrowing of the common hepatic duct 1-2 cm distal to the confluence, with the narrowing approximately 2 cm long, and also noted minor proximal biliary ductal dilatation.

treated with allogeneic stem cell transplant at an outside institution. The patient had been in remission for 4 years. The transplant was complicated by graft versus host disease, hemosiderosis, and chronic mild thrombocytopenia.

Initial work-up revealed a hyperbilirubinemia of 20.1 mg/dL, with direct and indirect bilirubin 14.2 and 5.9 mg/dL, respectively, alkaline phosphatase 319 U/L, alanine aminotransferase 96 U/L, aspartate aminotransferase 215 U/L, and a normal lipase. Magnetic resonance cholangiopancreatography (Figure 1) showed a narrow segment in the proximal common hepatic duct approximately 1-2 cm distal to the confluence. A subsequent ERCP confirmed the stricture. Brush biopsies remained nondiagnostic, and cholestasis was treated with placement of a biliary plastic stent. After ERCP, both symptoms and laboratory values improved, and the patient was discharged with a diagnosis of an indeterminate biliary stricture and acute cholangitis.

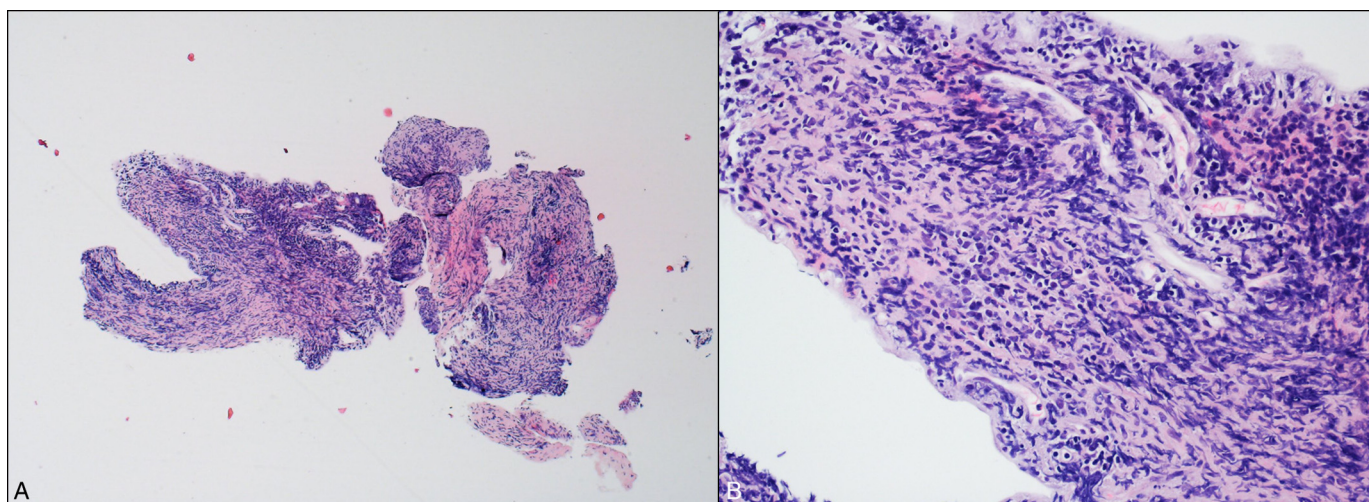
The patient presented 10 days later to our institution for further diagnostic management of the biliary stricture.



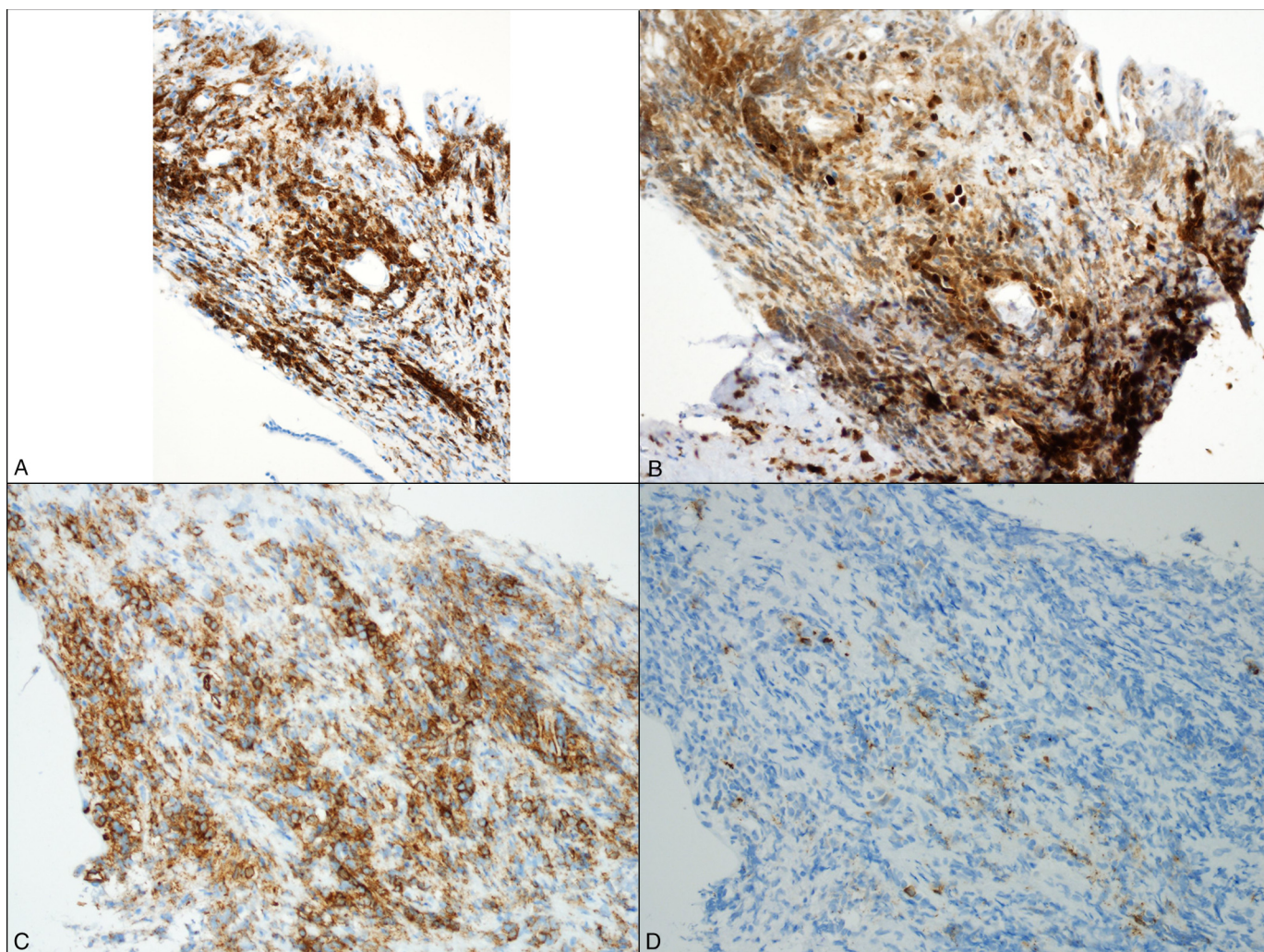
**Figure 2.** Endoscopic retrograde cholangiopancreatography showed common hepatic duct stricture of 2 cm with upstream bilateral intrahepatic ductal dilatation.

At that point, he denied fever, chills, or any other gastrointestinal symptoms. Vital signs were within normal limits. On physical exam, the patient was in no acute distress, with soft abdomen that was nondistended and nontender. Mild jaundice and mild scleral icterus were present. Laboratory work-up revealed a total bilirubin to 2.1 mg/dL, with direct bilirubin of 1.2 mg/dL and normal liver transaminases. Carbohydrate antigen 19-9 and carcinoembryonic antigen were within normal limits as well. A repeat ERCP confirmed a common hepatic duct stricture of 2 cm with upstream bilateral intrahepatic ductal dilatation (Figure 2). The biliary tree was swept with an 8.5-mm balloon. Resistance was met upon passing the inflated balloon through the stricture. Subsequent cholangioscopy (SpyGlass, Boston Scientific, MA) visualized nodularity and friability in the area of the stricture. Biliary brushing and fluorescence in situ hybridization remained nondiagnostic; however, a targeted biopsy with the Howell biliary introducer forceps (Cook Medical, NC) demonstrated infiltrating atypical mononucleated cells (Figure 3). Subsequent open biopsy of peritoneal nodules, cytology study of the peritoneal fluid, and bone marrow biopsy were performed. The flow cytometry analysis identified the blasts with mixed phenotype of both lymphoblasts and myeloblasts. With additional immunohistochemical studies, the blasts were positive for CD79a, terminal deoxynucleotidyl transferase, CD34, and CD10 and negative for myeloperoxidase (Figure 4). The profile confirmed the B-cell lineage of the blasts and a diagnosis of B-cell lymphoblastic leukemia was made.





**Figure 3.** Hematoxylin and eosin stain showing infiltrating atypical mononucleated cells at (A) 4x magnification and (B) 20x magnification.



**Figure 4.** Immunohistochemical studies testing positive for (A) CD79a, (B) TdT, (C) CD34, and (D) negative for myeloperoxidase.

## DISCUSSION

B-cell lymphocytic leukemia is a hematologic cancer that originates in the bone marrow and can metastasize to other organs. Previous case reports of lymphocytic leukemia have presented with cholestasis symptoms, but both were intrahepatic and diagnosed by liver biopsy.<sup>6,7</sup> A study of 6610 patients in MD Anderson Cancer Center to define the role of ERCP after hematopoietic stem cell transplant in patients presenting with jaundice, found that out of 40 patients that underwent ERCP, 17 had biliary strictures. From those 17, 76% (n = 13) were malignant.<sup>8</sup> Of note, malignant strictures presenting as recurrence of a primary hematologic malignancy occurred more frequently after autologous stem cell transplant than after an allogenic stem cell transplant.<sup>8</sup> Interestingly, this study did not demonstrate graft versus host disease as etiology for biliary strictures.

This case delineates the advantages of targeted biopsy with the use of the latest innovation in the field, high-resolution cholangioscopy in the work-up of indeterminate biliary strictures. This technique allows for detailed inspection of the biliary tree and facilitates targeted biopsies on lesions with malignant characteristics, such as irregular or tortuous vessels.<sup>9</sup> The increased diagnostic yield of high-resolution cholangioscopy is, however, hampered by its high costs and complication rate of 0.3%, including pancreatitis and cholangitis.<sup>10</sup>

## DISCLOSURES

Author contributions: All authors contributed equally to the manuscript. J. Melendez-Rosado is the article guarantor.

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